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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,621	08/24/2005	Thomas Rueckle	263675US0PCT	2551

22850 7590 05/30/2008

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EXAMINER	
KOSACK, JOSEPH R	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
05/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/520,621	RUECKLE ET AL.	
	Examiner	Art Unit	
	Joseph R. Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *7,10-16,20-23 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,17,18 and 28-34* is/are rejected.

7)☒ Claim(s) *19,24-27,35 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/19/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-37 are pending in the instant application.

Amendments

The amendment filed on February 19, 2008 has been acknowledged and has been entered into the application file.

Information Disclosure Statement

The Information Disclosure Statement filed February 19, 2008 has been considered fully by the Examiner.

Previous Claim Objections

Claims 1-6, 8-9, 17-19, 24-35, and 37 were previously objected to for containing elected and non-elected subject matter. As the elected species is still unpatentable and there as additional subject matter in the claims, the objection is maintained.

Previous Claim Rejections - 35 USC § 112

Claims 1-6, 8-9, 17-18 and 28-34 were previously rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Applicant has traversed the rejection on the grounds that they have found a group of compounds that are active on P13K and it appears not well balanced that the Applicant is required to provide all details of the administration.

Firstly, Applicant has not found compounds that are active on P13K, they have found compounds that are active on P13K-gamma. Most of the articles that Applicant has cited in their arguments and the IDS are drawn to P13K generically and do not mention P13K-gamma. Does this mean that the article describes all P13Ks? Does this

mean that if a compound inhibits P13K-gamma that that compound can inhibit all other P13Ks? No light is shed on these questions from the articles and the arguments. Additionally, Applicant does not address the definition given to prophylaxis used by the Examiner. It would seem that the compounds could not, for example, bar a bacterium from ever entering a human body and thereby cause an infection.

The articles do show clear support for the treatment of inflammation by the inhibition of P13K-gamma. Therefore, the rejection will be modified to show the enablement support for inflammation, but will be maintained for all other conditions.

Claim Objections

Claims 1-6, 8-9, 17-19, 24-35, and 37 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra. Applicant is advised that additional subject matter may be searched after all rejections are removed from the elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-9, 17-18 and 28-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of inflammation, does not reasonably provide enablement for treatment of any other disease. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

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The Nature of the Invention

The nature of the invention is the treatment of a wide variety of disorders ranging from autoimmune disorders to cancer to viral infections to cardiovascular disease.

The State of the Prior Art and the Predictability or Lack Thereof in the Art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the absence of clinical data to enable the invention, there needs to be a clear cause and effect relationship between inhibiting an enzyme and the effect that that inhibition causes. Applicant, while alleging that the compound can treat many widely varied diseases, fails to show that using the compound to inhibit PI3K would actually treat or prevent the diseases. While kinases have become more palatable targets of recent pharmaceutical research, there is a lot about the function of kinases that is unknown. In fact, Applicant states on page 7 of the disclosure that "it remains unclear which particular PI3K isoform or isoforms are involved in these phenomena." Applicant states that the intended target of the compounds is PI3K-gamma, a particular isoform of PI3K. Has it been shown in the art that inhibiting this particular isoform would treat or prevent the claimed diseases? Will inhibition have any effect on the human body? The documents cited by Applicant in the IDS of March 15, 2005 along with the disclosure do not shed much light on these questions. The IDS of February 19, 2008 does show support for inhibitors of P13K-gamma to treat inflammation. The person of skill who would practice this invention must know the answers or else they would require extensive undue experimentation to work out the proper doses to treat the claimed diseases.

Additionally, the claims are drawn to the prophylaxis of many various diseases. Prophylaxis includes the outright prevention of the diseases from even happening.

Prevention, if undefined by the specification, means that the condition or disease will *never* occur as a result of administration of the compound. For example, as the claims read now, this compound would prevent an infectious bacterium from ever entering the body, let alone cause any adverse symptoms. Also, different doses may be needed as a preventative than for treating a particular condition. Applicant does not provide guidance as to how the dosing would change if being given in a preventative dose.

Hence, in the absence of a showing of correlation in the art between all the diseases claimed as capable of treatment by antagonizing PI3K-gamma, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of antagonizing PI3K-gamma.

The Amount of Direction or Guidance Present and the Presence or Absence of Working Examples

The specification provides an assay for PI3K-gamma activity for particular compounds of the invention on page 121 of the disclosure, but do not show any evidence of the effectiveness at treating or preventing diseases.

The Breadth of the Claims

The breadth of the claims is the treatment of various diseases, whether or not they are mediated by PI3K-gamma inhibition.

The Quantity of Experimentation Needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine the proper dose to deliver to a patient to treat a claimed disease with no knowledge as to how inhibiting PI3K-gamma actually treats the disease.

The Level of Skill in the Art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of claim 1 for the treatment of diseases mediated by antagonizing PI3K-gamma. As a result, necessitating one of skill to perform an exhaustive search for which diseases can actually be treated by what compounds of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome deleting the claims or by amending the claims to be limited to treating (not preventing) diseases that have a *clear* correlation to inhibiting (antagonizing) PI3K-gamma.

Conclusion

Claims 1-6, 8-9, 17-18 and 28-34 are rejected. Claims 1-6, 8-9, 17-19, 24-35, and 37 are objected to.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rebecca L Anderson/
Primary Examiner, Art Unit 1626

/Joseph R Kosack/
Examiner, Art Unit 1626